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PRINCIPAL INVESTIGATOR: Maureen Sanderson, Ph.D.

CONTRACTING ORGANIZATION: Meharry Medical College
Nashville, TN 37208

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Maureen Sanderson

**E-Mail:** msanderson@mmc.edu

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**14. ABSTRACT**

The purpose of this HBCU/MI Partnership Training Award is to train Meharry Medical College faculty to conduct independent breast cancer research by collaborating with faculty from Vanderbilt University Medical Center. Year 1 is a training year and during Years 2 through 4 a case-control study of obesity, insulin resistance and mammographic breast density will be conducted. Specific aims include: 1) to assess mammographic breast density through digital mammograms; for a sample of women we will also assess mammographic breast density through film mammograms to determine the diagnostic accuracy of digital versus film mammogram, 2) to obtain information on breast cancer risk factors including health literacy, and to collect anthropometric measurements and fasting blood, 3) to assay blood for select hormones and growth factors, 4) to perform statistical analyses to determine the associations between obesity and insulin resistance and mammographic breast density, and 5) to evaluate patients' ability to understand their mammogram findings as they are explained by their medical provider. Dr. Sanderson attended several conferences including Era of Hope, Dr. Jones attended a community engagement conference and took coursework, and Dr. Khoder attended a breast cancer research conference. Institutional review board approval was obtained for the mammographic breast density study.

**15. SUBJECT TERMS**
Epidemiology/biostatistics, hormone metabolism

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**Introduction**

The purpose of this HBCU/MI Partnership Training Award is to train Meharry Medical College (MMC) faculty to conduct independent breast cancer research by collaborating with faculty from Vanderbilt University Medical Center (VUMC). Three MMC faculty will undergo intensive training supervised by three VUMC faculty during year 1 with additional training taking place in subsequent years. To reinforce training, faculty from MMC and VUMC will conduct a case-control study of mammographic breast density to investigate its' association with obesity and insulin resistance in years 2 through 4. Cases (n=150) whose breasts are in the upper quartile of breast density and controls (n=850) whose breast are in the lowest three quartiles of breast density, will be recruited from the MMC Center for Women's Health Research which serves a medically underserved population. Specific aims are: 1) to assess mammographic breast density through digital mammograms; for a sample of women we will also assess mammographic breast density through film mammograms to determine the diagnostic accuracy of digital versus film mammogram, 2) to obtain information on breast cancer risk factors including health literacy, and to collect anthropometric measurements and fasting blood, 3) to assay blood for select hormones and growth factors, 4) to perform statistical analyses to determine the associations between obesity and insulin resistance and mammographic breast density, and 5) to evaluate patients' ability to understand their mammogram findings as they are explained by their medical provider.

**Body**

Dr. Maureen Sanderson replaced Dr. Alecia Fair as MMC Principal Investigator (PI) of the project effective July 11, 2011. As indicated in the Statement of Work (Appendix), this project is occurring in two phases, the training phase (year 1) and the investigation phase (years 2 through 4). During the first year of the project, we partially completed training task 1a by Dr. Sanderson attending the American Association for Cancer Research (AACR) Cancer Health Disparities Conference, and by presenting posters at the American Public Health Association Conference, the Society for Epidemiologic Research Conference, and the Department of Defense Era of Hope Conference (Appendix includes abstracts for the current study and Dr. Sanderson's previous study DAMD17-03-1-0274); by Dr. Jones presenting a poster at the Clinical and Translational Science Award Community Engagement Conference (Appendix includes abstract); and by Dr. Khoder attending the AACR Advances in Breast Cancer Research Conference. We partially completed training task 1b by Dr. Jones taking Epidemiology, Fundamental Principles of Human Research, Biostatistics, Social and Behavioral Science for Public Health, Research Ethics, Molecular Medicine, Communications/Grant Writing, and Clinical Trials in the Master's of Science in Clinical Investigation (MSCI) Program. We completed training task 1c by meeting with Drs. Richard-Davis, Disher, Al-Hendy and Mouton from the MMC Center for Women's Health Research to design the breast density study to include digital mammogram assessment, completion of a questionnaire, anthropometry and a blood draw. We completed training tasks 1d through 1l by developing a questionnaire appropriate for use with the local population; designing the protocols for subject recruitment, data collection, laboratory work, tracking system, data entry programs, and by writing the manual of operations. We obtained Institutional Review Board (IRB) approval initially from MMC on 9/7/2010, VUMC on 6/7/2011, and the Department of Defense (DOD) on 6/27/2011. Drs. Dupont, Shu and Peterson from VUMC provided input on the poster presented at the Era of Hope Conference and the questionnaire.

During the second year of the project, we will move from the training phase into the investigation phase. We will partially complete training task 1b by Dr. Jones continuing to take coursework toward completion of the MSCI degree. Drs. Sanderson and Khoder will attend workshops and conferences when possible. We have hired a full-time project coordinator and half-time research assistant and anticipate beginning subject recruitment and data collection by the end of October, 2011. We will partially or fully complete investigation tasks 2 through 8. Investigation task 9 will be completed in subsequent years.

**Key Research Accomplishments**

- Partially completed training task 1a by Drs. Sanderson, Jones and Khoder attending and/or presenting posters at workshops and conferences.

- Partially completed training task 1b by Dr. Jones taking coursework in the MSCI Program.

- Completed training task 1c by consulting with our advisory board and health providers in the MMC Center for Women's Health Research to design the breast density study.

- Completed training tasks 1d through 1l by developing study protocols, posters, informed consent documents, standard operating procedures, questionnaires and databases, and by obtaining IRB approval from three entities.

**Reportable Outcomes**

1) Manuscripts

Not applicable

2) Abstracts

Sanderson M, Fair AM, Jones C, Khoder W, Dupont W, Shu XO, Peterson N. Mammographic breast density in a cohort of medically underserved women. 6th Department of Defense Breast Cancer Research Program Era of Hope Meeting, Orlando, FL, August 2011.

Sanderson M, Weriwoh M, Peltz, Perez A, Johnson M, Fadden MK. Perinatal factors and breast cancer risk among Latinas. 6th Department of Defense Breast Cancer Research Program Era of Hope Meeting, Orlando, FL, August 2011.

Jones CD, Pryor JL. A combination of marketing and information technology to grow community awareness and to expedite translational research projects. 4th Annual National CTSA Community Engagement Conference, Bethesda, MD, August 2011.

3) Grants

Not applicable

**Conclusions**

The overall goal of this proposed HBCU/MI Partnership Training Award is to strengthen the existing collaborative relationship between the minority institution, MMC, and the collaborating institution, VUMC. The investigators from MMC and VUMC have mutual interests in studying the interplay of lifestyle and molecular factors on breast cancer risk as measured by its precursor, mammographic breast density. High mammographic breast density is comparable in its predictive magnitude of risk to historically well-established breast cancer risk factors. The biological basis for the association between higher percentage of density and risk of breast cancer is not clear but may be related to increased stroma and glandular tissue in dense breasts through estrogen exposures or production of certain growth factors including insulin-like growth factor-I (IGF-I) or adipokines such as leptin. Very few studies have focused on obesity and insulin resistance as they relate to mammographic breast density. We hypothesize that: 1) obesity and insulin resistance, defined as high levels of C-peptide, will be positively associated with high mammographic breast density, and 2) these associations will be more pronounced among women with high levels of IGF-I and high levels of leptin.

This project will establish associations between some lifestyle and molecular factors and mammographic breast density; known to be linked to subsequent breast cancer, especially in minority and medically underserved women. By identifying biomarkers that influence mammographic breast density in minority women, this project may provide therapeutic targets for new prevention strategies in this population. While faculty from VUMC has expertise in breast cancer research, faculty from MMC has strong ties with minority communities in Nasvhille and Davidson County. To date, limited breast cancer research has been conducted at MMC. By partnering together, MMC and VUMC hope to build infrastructure to conduct population-based case-control studies of breast cancer at MMC, and to establish an outstanding collaborative breast cancer research program.

**References**

Sanderson M, Weriwoh M, Peltz G, Perez A, Alexander L, Fadden MK, Agboto V. Perinatal factors and breast cancer risk among Hispanic women (Under review).

**Statement of Work**

Phase 1: Training Phase (Year 1)

**Task 1:** (Drs. Sanderson, Khoder, Jones, Richard-Davis, Disher, Sanderson, Dupont, Peterson and Shu)

1a. Drs. Sanderson, Khoder and Jones audit courses at Summer Research program at University of Michigan (months 6-7).
1b. Dr. Jones begins the Meharry Medical College, Master's of Science in Clinical Investigation Program (months 1-30).
1c. Consult with advisory board and health providers in the Center for Women's Health Research (CWHR) to design a cross-sectional study for measurement of mammographic breast density, related hormones and health literacy (months 1-3).
1d. Develop and finalize study protocol for recruitment of participants (months 1-6).
1e. Develop and finalize study protocol for obtaining analog screening mammograms and digital mammograms (months 1-3).
1f. Finalize advertisements for contacting participants, questionnaires, and other data collection forms (months 1-3).
1g. Order supplies for blood collection and processing, order supplies for performing assays (months 5-6).
1h. Create and finalize quality assurance audit forms to ensure safety of participants and integrity of all data (months 4-6).
1i. Update IRB protocols, informed consent documents, and HIPAA waivers for IRB submission (months 4-6).
1j. Generate standard operating procedures manual to reflect all aspects of study procedures (months 4-6).
1k. Work with Dr. Dupont to modify accrual database to include scripts and screening forms, and allow accrual and productivity reports to be generated (months 7-12).
1l. Work with the project coordinator to create REDCAP database for entry of study data (months 7-12).

Phase 2**:** Investigation Phase (Years 1 through 4)

**Specific Aim 1)** to assess mammographic breast density through digital mammograms; for a sample of women we will also assess mammographic breast density through analog mammograms to determine the efficacy of digital versus analog mammogram;

**Specific Aim 2)** to obtain information on breast cancer risk factors including health literacy, and to collect anthropometric measurements and fasting blood;

**Specific Aim 3)** to assay blood for select hormones and growth factors;

**Specific Aim 4)** to perform statistical analyses to determine the association between obesity and insulin resistance and mammographic breast density;

**Specific Aim 5)** to evaluate patients' ability to understand their mammogram findings as they are explained by their medical provider.

**Task 2:** (Drs. Sanderson, Dupont, Disher, Khoder)
Quantitate mammographic breast density measurement, Months 1-42.

2a. Work with Dr. Disher to refine protocols for mammographic density analyses (months 1-12).
2b. Work with Dr. Disher to observe Cumulus computer program to quantify breast density (months 7-12).
2c. Coordinate flow of digital mammography data from the Center of Women's Health Research to Dr. Disher for quantitation (months 7-42).
2d. Assess breast density of mammograms using digital quantitative analysis to obtain the percentage of the breast occupied by breast tissue (months 7-42).

**Task 3**: (Drs. Sanderson, Jones, Disher)
Recruit subjects and collect data, Months 7-42.

3a. Screen and recruit potentially eligible women for digital mammography study at the Center for Women's Health Research (1,000 patients total) (months 7-42).
3b. Administer questionnaire (months 7-42).
3c. Perform standardized body measures; weight, height, skinfold thickness, and waist and hip circumference (months 7-42).
3d. Collect blood samples and transport to Vanderbilt molecular epidemiology laboratory for storage and processing (months 7-42).
3e. Order additional supplies as needed (months 7-42).

**Task 4:** (Drs. Jones, Khoder and Peterson**)** Months 7-42.

4a. Administer Short Test of Functional Literacy in Adults **(**S-TOFHLA) to study participants (months 7-42).
4b. Score S-TOFHLA instruments and categorize levels of patient's health literacy (months 7-42).

**Task 5:** (Drs. Sanderson, Jones, Khoder and Shu)
Process blood samples, measurements and perform stated assays, Months 7-42.

5a. Supervise research staff in acquisition and analysis of data (months 7-42).
5b. Separate serum, plasma and clot in blood sample and store at -80°C (months 7-42).
5c. Transport biospecimens to the Vanderbilt University molecular epidemiology laboratory for processing and analysis (months 7-42).

**Task 6:** (Drs. Khoder, Disher and Dupont) Months 7-42.

6a. Obtain analog mammography films and digital mammography films for each participating patient for rating of quantitative breast density by interpretation (months 7-42).
6b. Calculate the sensitivity and specificity of each modality for detecting mammographic breast density (months 7-42).
6c. Perform statistical analyses to account for multiple comparisons in breast density subgroups (months 40-42).

**Task 7:** (Drs. Sanderson, Jones, Khoder **,** Dupont)

Conduct ongoing quality assurance audits to ensure patient safety and data integrity, Months 7-48. Twice monthly monitoring of activities (number of screening phone calls logged, number and type of contacts with potential or actual participants, progress with data entry, etc.).

7a. Twice monthly monitoring of study accrual (months 7-42).

7b. Continuous monitoring/reporting of potential adverse events (months 7-48).

7c. Monthly audits to verify study staff adherence to standard operating procedures (months 7-48).

**Task 8: (**Drs. Sanderson, Jones, Khoder, Shu, Dupont, Peterson)

Conduct interim analyses, Months 12-48.

8a. Perform interim statistical analysis (months 12-18, months 24-30, months 36-42).

8b. Preparation and submission of abstracts reflecting findings to date (months 36-48).

8c. Creation and submission of annual reports to funding agency (months 12, 24, 36).

**Task 9:** (Drs. Sanderson, Jones, Khoder, Shu, Dupont, Peterson)

Final analyses and dissemination of data, Months 22-48.

9a. Begin final statistical analyses (months 40-48).

9b. Preparation and submission of final report to funding agency (months 48).

9c. Preparation and submission of abstracts and manuscripts reflecting final results (months 40-48).

**Mammographic breast density in a cohort of medically underserved women**

M. Sanderson, A.M. Fair, C. Jones, W. Khoder, W. Dupont, X.O. Shu, N. Peterson

Background: High mammographic breast density is comparable in its predictive magnitude of risk to historically well-established breast cancer risk factors. The biological basis for the association between higher percentage of density and risk of breast cancer is not clear but may be related to increased stroma and glandular tissue in dense breasts through estrogen exposures or production of certain growth factors including insulin-like growth factor-I (IGF-I) or adipokines such as leptin. Very few studies have focused on obesity and insulin resistance as they relate to mammographic breast density.

Hypotheses: We hypothesize that: 1) obesity and insulin resistance, defined as high levels of C-peptide, will be positively associated with high mammographic breast density, and 2) these associations will be more pronounced among women with high levels of IGF-I and high levels of leptin.

Specific Aims: The specific aims of the proposed clinic-based case-control study of mammographic breast density are: 1) to assess mammographic breast density through digital mammograms; for a sample of women we will also assess mammographic breast density through film mammograms to determine the diagnostic accuracy of digital versus film mammogram, 2) to obtain information on breast cancer risk factors including health literacy, and to collect anthropometric measurements and fasting blood, 3) to assay blood for select hormones and growth factors, 4) to perform statistical analyses to determine the associations between obesity and insulin resistance and mammographic breast density, and 5) to evaluate patients' ability to understand their mammogram findings as they are explained by their medical provider.

Study Design: The proposed project, a clinic-based case-control study, will be conducted in MMC's Center for Women's Health Research (CWHR) utilizing a digital mammography system with the mammography reporting system. Cases will be defined as women whose breasts are in the upper quartile of breast density (n=150), while controls will be defined as women whose breasts are in the lowest three quartiles of breast density (n=850).

Impact: This research will establish the role of mammographic breast density and associated factors in breast cancer risk for minority and medically underserved populations and may provide data needed to allow minority women to make informed decisions about breast cancer prevention. Further, by identifying biomarkers influencing mammographic breast density in minority women, this research may provide therapeutic targets for new prevention strategies in this population. Given the known differences in breast cancer in minority populations relative to the general population, this research will address an important issue that will ensure that early detection strategies are equally effective in all women.

**Perinatal factors and breast cancer risk among Latinas**

M. Sanderson, M. Weriwoh, G. Peltz, A. Perez, L. Alexander, M.K. Fadden, V. Agboto

Birthweight and other perinatal factors have been linked to subsequent breast cancer. These associations have yet to be investigated among Latina women who have fairly low rates of breast cancer. In the current study, we assessed whether perinatal factors were associated with breast cancer among Latinas. We used data from a case-control study of breast cancer among Latina women age 30 to 79 conducted between 2003 and 2008 on the Texas-Mexico border. In-person interviews were completed with 190 incident breast cancer cases ascertained through surgeons and oncologists, and 979 controls who were designated as high-risk (n=511) and low-risk (n=468) for breast cancer (with respective response rates of 97%, 83% and 74%). Women who were adopted were excluded and perinatal factors were based on self-report. There was no evidence of confounding by age, menopausal status or body mass index. Relative to birthweight 2,500-3,999 grams, there was no association with breast cancer risk for birthweight of <2,500 grams (odds ratio [OR] 0.84, 95% confidence interval [CI] 0.52-1.35) or 4,000+ grams (OR 0.63, 95% CI 0.33-1.21). Nor was there an association between maternal age (25-29 years OR 0.84, 95% CI 0.54-1.31; 30+ years OR 0.73, 95% CI 0.49-1.08 relative to <25 years) or birth order (2+ OR 0.99, 95% CI 0.67-1.46 relative to 1) and breast cancer. However, there was a significant increase in breast cancer risk among women whose mothers smoked during pregnancy (OR 1.73, 95% CI 1.04-2.88). With the exception of birth order, our results differed from previous studies of this topic. The non-significant reductions in breast cancer risk associated with birthweight were unexpected since a recent pooled analysis reported no association for <2,500 grams and a weak positive association for 4,000+ grams. Our findings for maternal age and maternal smoking differed from a recent meta analysis which reported odds ratios of around 1.2 and 1.0, respectively for case-control studies. We were unable to examine prematurity, twinship or maternal hormone use because fewer than 30 women exhibited these exposures. Our study is the first study to investigate the association between perinatal factors and breast cancer among Latina women. A possible explanation for our findings is the different hormonal milieu among Latinas relative to Caucasian, African American and Asian women in whom all previous studies of this topic have been conducted. The confirmation of our findings in larger studies may assist in determining how hormonal mechanisms responsible for breast cancer differ by race/ethnicity.

**A combination of marketing and information technology to grow community awareness and to expedite translational research projects**

C.D. Jones, J.L. Pryor

The Meharry Translational Research Center (MeTRC) is a long-range endeavor to design and implement translational research and its-related training infrastructure at Meharry Medical College. MeTRC aims to incubate critical research questions and produce well-trained scientists ready to confront health disparities through independent research funding. The integrated training and enhanced research infrastructure provided by MeTRC aims to fully balance research across the bench-to-bedside-to-community continuum. To grow internal and external community awareness of MeTRC, the Collaborations and Partnerships Core hosted an open house. The specific aim of this event was to expand knowledge about the availability of MeTRC core resources and funding and to bring together key stakeholder and community organization for the advancement of health care objectives. One component that MeTRC has developed to achieve this goal is the intranet web portal, ResearchPoint, unveiled during the open house. ResearchPoint aims to support the success of Meharry Research, from idea to grant, technology transfer to implementation, by supplying resources and useful information to researchers such as forms, upcoming events, support activities, and a help service for the submission process. Since ResearchPoint's debut, support and tools for grant submissions are found in a centralized location, and new applications are only accepted online via ResearchPoint. The use of this intranet site cultivates research that expedites translation of discoveries into novel therapeutic options for the community. The open house engaged the Meharry community and external organizations as well as provided pertinent information to the stakeholders in attendance. The intranet site, ResearchPoint, was unveiled and is transforming the inception of research at Meharry. To date MeTRC has received 99 application and has funded 25 projects resulting in 15 scholarly publications. The areas of influence for improved health outcomes included HIV, dental health, and diabetes, among others.